oligonucleotide is an α-anomeric oligonucleotide. An α-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gautier *et al.*, *Nucl. Acids. Res.* 15:6625, 1987). The oligonucleotide is a 2'-0-methylribonucleotide (Inoue *et al.*, *Nucl. Acids Res.* 15:6131, 1987), or a chimeric RNA-DNA analog (Inoue *et al.*, *FEBS Lett.* 215:327, 1987).

Antisense oligonucleotides of the invention can be synthesized by standard methods known in the art, for example, by use of an automated DNA synthesizer (such as are commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides can be synthesized by the method of Stein *et al.* (*Nucl. Acids Res.* 16:3209, 1988), and methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin *et al.*, *Proc. Natl. Acad. Sci. USA* 85:7448, 1988).

For therapeutic application, antisense molecules of the invention should be delivered to cells that express GLUTX *in vivo*. A number of methods have been developed for delivering antisense DNA or RNA to cells; for example, antisense molecules can be injected directly into the tissue site. Alternatively, modified antisense molecules, which are designed to target cells that express GLUTX (*e.g.*, antisense molecules linked to peptides or antibodies that specifically bind receptors or antigens expressed on the target cell surface) can be administered systemically.

However, it is often difficult to achieve intracellular concentrations of antisense molecules that are sufficient to suppress translation of endogenous mRNAs. Therefore, a preferred approach uses a recombinant DNA construct in which the antisense oligonucleotide is placed

under the control of a strong *pol* III or *pol* II promoter. The use of such a construct to transfect target cells in the patient will result in the transcription of sufficient amounts of single stranded RNAs that will form complementary base pairs with endogenous GLUTX transcripts and thereby prevent translation of GLUTX mRNA. For example, a vector can be introduced *in vivo* in such a way that it is taken up by a cell and thereafter directs the transcription of an antisense RNA. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA.

Vectors encoding a GLUTX antisense sequence can be constructed by recombinant DNA technology methods that are standard practice in the art. Suitable vectors include plasmid vectors, viral vectors, or other types of vectors known or newly discovered in the art. The criterion for use is only that the vector be capable of replicating and expressing the GLUTX antisense molecule in mammalian cells. Expression of the sequence encoding the antisense RNA can be directed by any promoter known in the art to act in mammalian, and preferably in human, cells. Such promoters can be inducible or constitutively active and include, but are not limited to: the SV40 early promoter region (Bernoist *et al.*, *Nature* 290:304, 1981); the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto *et al.*, *Cell* 22:787-797, 1988); the herpes thymidine kinase promoter (Wagner *et al.*, *Proc. Natl. Acad. Sci. USA* 78:1441, 1981); or the regulatory sequences of the metallothionein gene (Brinster *et al.*, *Nature* 296:39, 1988).

VI. Ribozymes

Ribozyme molecules designed to catalytically cleave GLUTX mRNA transcripts also can be used to prevent

translation of GLUTX mRNA and expression of GLUTX polypeptides (see, for example, PCT Publication WO 90/11364; Saraver *et al.*, *Science* 247:1222, 1990). While various ribozymes that cleave mRNA at site-specific recognition sequences can be used to destroy GLUTX mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of hammerhead ribozymes is well known in the art (Haseloff *et al.*, *Nature* 334:585, 1988). There are numerous examples of potential hammerhead ribozyme cleavage sites within the nucleotide sequence of human GLUTX cDNA. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the GLUTX mRNA, *i.e.*, to increase efficiency and minimize the intracellular accumulation of non-functional mRNA transcripts.

The ribozymes of the present invention also include RNA endoribonucleases (hereinafter "Cech-type ribozymes"), such as the one that occurs naturally in *Tetrahymena Thermophila* (known as the IVS or L-19 IVS RNA), and which has been extensively described by Cech and his collaborators (Zaug *et al.*, *Science* 224:574, 1984; Zaug *et al.*, *Science* 231:470, 1986; Zug *et al.*, *Nature* 324:429, 1986; PCT Application No. WO 88/04300; and Been *et al.*, *Cell* 47:207, 1986). The Cech-type ribozymes have an eight base-pair sequence that hybridizes to a target RNA sequence, whereafter cleavage of the target RNA takes place. The invention encompasses those Cech-type ribozymes that target eight base-pair active site sequences present in GLUTX.

As in the antisense approach, the ribozymes can be